Perfusion Imaging of Hemangioblastoma: Implications for using Arterial Spin Labeling to Characterize Tumor Hemodynamics

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Introduction

Arterial spin labeling (ASL) MRI has become a standard technique for measuring cerebral blood flow (CBF) and is a logical choice for imaging flow-altering neuropathology. In this preliminary study, we took a multiple subtraction (MS) ASL approach to investigate perfusion dynamics in hemangioblastoma, a highly vascular tumor. Inflow curves for arterial, gray matter (GM), and tumor regions are presented, with the general kinetic model (GKM) for quantitative ASL applied (1). We subsequently discuss implications for using MS ASL to evaluate tumor blood flow (TBF) and vascularity, and provide advantages over a single subtraction (SS) model.

Methods

Two human subjects previously diagnosed with hemangioblastomas were imaged. Pulsed ASL experiments using the PICORE tagging scheme were performed on a Siemens 3T Trio scanner, equipped with an 8-channel imaging coil. The imaging sequence was modified to cycle through a range of inversion times (TIs) in a single scan; this "TI stepping" allowed characterization of the entire bolus inflow curve. The imaging parameters were TI = 50 ms to 1700 ms, in increments of either 150 ms or 200 ms; tag width = 100 mm; gap between imaging volume and inversion slab = 20 mm; TR = 2-3 sec; FOV = 225 mm; 64x64 matrix; 120 - 240 measurements; slice thickness = 5mm; interslice gap = 2.5 mm; and scan time = 6 – 8 min. Six axial slices were positioned to give coverage of the entire tumor volume.

MS analysis was consistent for both experiments. Perfusion-weighted maps were generated by subtracting tag images from control images and correcting with the M_{OB} magnetization calibration constant (2). Maps at a single TI were averaged together to produce a single map for each TI. Regions of interest were drawn in a GM gyrus, a middle cerebral artery (MCA) branch, and the hemangioblastoma. Signal intensities from voxels within an ROI were averaged and plotted versus TI. This inflow plot was fit with the GKM and perfusion parameters were reported.

Patient 1

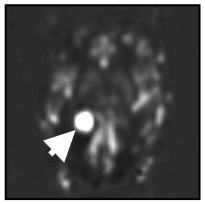

Figure 1. Perfusion Map from patient 1. White arrow points to tumor.

Table 1	*f (ml/100g-min)*	Δt (ms)	τ (ms)
Tumor	**448.9**	**151**	**1040**
GM	**57.8**	**669**	**810**
MCA	**581.7**	**66**	**400**

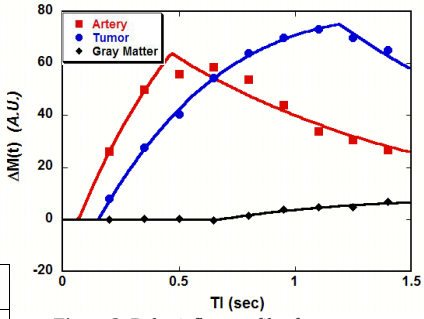

Figure 2. Bolus inflow profiles for artery, tumor, and gray matter in patient 1, fit with GKM.

Patient 2

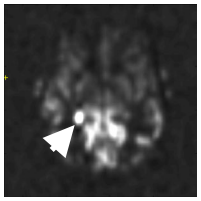

Figure 3. Perfusion Map from patient 2. White arrow points to tumor.

Table 2	*f (ml/100g-min)*	Δt (ms)	τ (ms)
Tumor	**250.0**	**117**	**1024**
GM	**50.3**	**588**	**702**
MCA	**261.6**	**35**	**492**

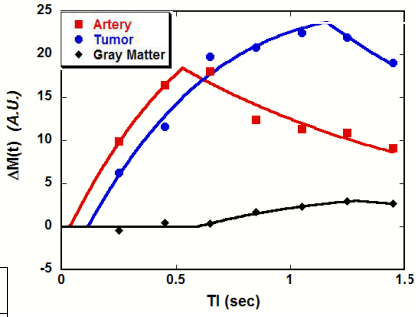

Figure 4. Bolus inflow profiles for artery, tumor, and gray matter in patient 2, fit with GKM.

Results and Discussion

Figures 1 and 3 show representative perfusion maps for patient 1 and 2, respectively. Figure 2 and 4 show bolus inflow curves for ROI's drawn in the tumor, GM, and MCA branch of patients 1 and 2, respectively. Tables 1 and 2 summarize flow parameters **Δ**t, **τ**, and ***f***, for patients 1 and 2, respectively. In this application, **Δ**t represents the transit delay, the interval between inversion and tagged spin arrival at the imaging slice (i.e., when **Δ**M = 0). **τ** represents the net delivery period, the interval during which tagged spin delivery dominates venous clearance and T1 decay (i.e., when **Δ**M increases), and ***f*** is the calculated blood flow.

Bolus inflow parameter values were as expected for arterial and gray matter regions. The tumor inflow curve describes a short transit delay and high blood flow, with a comparatively long delivery time. The combination of these properties is unusual; the short transit delay and steep rise in longitudinal magnetization (**Δ**M) suggest that tagged blood delivery to the tumor is initially rapid with a high flow, similar to the artery. The long delivery time (**τ**), however, suggests that within the tumor, delivery dominates clearance and decay for an extended period of time, even longer than GM. This result is inconsistent with normal brain physiology. Normally, if tagged blood arrives at the imaging slice at such a high rate, the entire bolus would be delivered rapidly and cleared, effects of venous clearance and T1 decay would dominate earlier, and **Δ**M would start decreasing sooner (**τ** would be short). These data therefore suggest that venous clearance of tagged blood from the tumor is somehow delayed, resulting in tagged blood remaining in the tumor cross-section for an extended duration. Hemangioblastoma pathophysiology may provide the explanation.

Hemangioblastomas are slow-growing tumors of endothelial origin with a solid component composed of tightly packed blood vessels. The blood vessels vary in size from capillary to cavernous and, like other vascular tumors, often have tortuous vessel patterns (3). The extensive capillary network, denser than GM, is characteristic for hemangioblastoma, and offers a logical way for tagged blood to remain within the tumor despite high flow from feeding vessels, since inverted blood entering a capillary bed takes at least one second to traverse the vascular tree and exit (1). Vessel tortuousity may also be a contributing factor, as tumor marcrovessels entering the imaging plane may circulate within the plane for a finite time before exiting. Cavernous vasculature could lead to tagged blood pooling within the tumor, thereby preventing re-entry into the circulation. In all these situations, venous clearance would be delayed, resulting in a longer net delivery time.

Our results show the importance of doing a full MS ASL characterization for the study of vascular tumors. Had a SS approach been taken, the unique results confirming tumor vessel heterogeneity would have been completely missed, since only the ***f*** parameter would have been measured. The data from both patients suggest that structures with similar flow values may in fact have very different hemodynamics (compare artery and tumor). The MS approach provides the additional delivery parameters **Δ**t and **τ**, which give important information about tumor vessel heterogeneity. Furthermore, because calculated flow (***f***) will underestimate real flow in high flow situations (1), **Δ**t and **τ** may become the most useful parameters for tumor assessment with ASL.

Conclusion

Because of vessel heterogeneity, tumors can simultaneously display properties of macrovascular flow and capillary perfusion, and thus be well characterized with ASL delivery parameters. In theory, measurement of the delivery parameters **Δ**t, **τ**, and ***f*** could provide an effective way to measure tumor vascularity and capillary density. These parameters could be combined mathematically to provide an ASL tumor "score", which could be used for tracking tumor progression, evaluating response to therapy, or assessing malignant potential, and could be very useful in clinical management. Furthermore, different classes of tumors may have different parameter value ranges, based on their inherent structure. In this setting, MS ASL could be developed as a non-contrast method for tumor identification and classification.

References: 1) Buxton et al., MRM 40: 383-396 (1998), 2) Wong et al., MRM 39:702 (1998), 3) Urena et. al., eMedicine.com, Hemangioblastoma, Brain, 2004.

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